510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k060998

B. Purpose for Submission:

New device

C. Measurand:

Tobramycin

D. Type of Test:

Quantitative particle-enhanced turbidimetric immunoassay

E. Applicant:

Seradyn, Inc.

F. Proprietary and Established Names:

QMS Tobramycin

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.3900

2. Classification:

   Class II

3. Product code:

   LCR - Fluorescent Immunoassay Tobramycin

4. Panel:

   Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See Indications for use.

2. Indication(s) for use:
   The QMS® Tobramycin assay is for the quantitative determination of tobramycin in human serum or plasma on automated clinical chemistry analyzers.

   The results obtained are used in the diagnosis and treatment of tobramycin overdose and in monitoring levels of tobramycin to help ensure appropriate therapy.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:
   Clinical chemistry analyzers . Performance was established on The Roche Hitachi 917 analyzer.

I. Device Description:

The QMS® Tobramycin assay consists of reagents R1: <0.2% anti-tobramycin monoclonal antibody (purified from mouse ascites) in a buffer with <0.09% sodium azide as preservative and R2: <0.3% tobramycin-coated microparticles in buffer containing stabilizer and <0.09% sodium azide as preservative

The calibrators were previously cleared under k872349.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Abbott TDx/TDx Flx Tobramycin assay (originally cleared as Cybrex Tobramycin)

2. Predicate 510(k) number(s):

   k802668

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	The QMS Tobramycin assay is for the quantitative determination of tobramycin in serum or plasma.	TDx/TDxFlx Tobramycin assay is a reagent system for the quantitative measurement of tobramycin, an aminoglycoside antibiotic drug, in serum or plasma.
Analyte	Tobramycin	Same
Matrix	Serum or Plasma	Same
Storage	2-8 °C	Same
Differences		
Item	**Device**	**Predicate**
Methodology	Homogeneous particle-enhanced turbidimetric immunoassay	Fluorescence Polarization (FPIA)
Reagents	2	3

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods
CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach
CLSI EP7-A: Interference Testing in Clinical Chemistry
CLSI EP9-A: Method Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

The QMS Tobramycin assay is a homogeneous particle-enhanced turbidimetric immunoassay. The assay is based on competition between drug in the sample and drug coated onto a microparticle for antibody binding sites of the tobramycin antibody reagent. The tobramycin-coated microparticle reagent (R2) is rapidly agglutinated in the presence of the anti-tobramycin antibody reagent (R1) and in the absence of any competing drug in the sample. The rate of absorbance change is measured photometrically and is inversely proportional to the rate of agglutination of the particles. When a sample containing tobramycin is added, the agglutination reaction is partially inhibited, slowing down the rate of absorbance change. A concentration-dependent agglutination inhibition curve can be obtained with maximum rate of agglutination at the lowest tobramycin concentration and the lowest agglutination rate at the highest tobramycin concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

Precision was conducted and assessed according to NCCLS EP5-A2.Three commercially available control materials (Low Control, Mid Control, and High Control) were evaluated on the Hitachi 917 and, after 2 hours within the same day, the samples were re-run in duplicate, over 20 days resulting in a total of 80 replicates for each control. Calibration was performed initially and re-calibration was performed when the controls did not recover within labeled ranges. The results for the precision study are presented below.

Precision on the Hitachi 917

			Within Run		Between Day		Total	
	N	Mean	SD	CV%	SD	CV%	SD	CV%
Low Control	80	1.11 µg/mL	0.022	1.98	0.054	4.86	0.084	7.57
Mid Control	80	3.83 µg/mL	0.050	1.31	0.120	3.13	0.162	4.23
High Control	80	8.06 µg/mL	0.131	1.63	0.057	0.71	0.343	4.26

b. *Linearity/assay reportable range:*
The reportable range of the assay is 0.4 – 10 µg/mL.

Linearity was assessed by following the CLSI EP6-A guideline. A stock solution of approximately 17 ug/mL tobramycin in a human serum pool was diluted with human serum negative for tobramycin to achieve samples across and above the reportable range of the assay (0.4-10 ug/mL). These samples were run in triplicate and the percent recovery for each sample was determined by dividing the mean observed result by the theoretical value. The results were evaluated by linear regression. The results are summarized below.

Theoretical Concentration (µg/mL)	Mean Recovered Concentration	SD	CV %	% Recovery
0.465	0.48	0.055	11.395	104.05
0.929	0.91	0.067	7.3437	97.60
1.858	1.82	0.030	1.6484	97.95
3.716	3.53	0.021	0.5892	95.08
5.574	5.47	0.047	0.8634	98.19
7.432	7.33	0.079	1.0828	98.63
9.290	9.29	0.066	0.7059	100.00
11.148	11.04	0.071	0.6428	99.00
13.006	13.00	0.095	0.7272	99.93

Theoretical Concentration (μg/mL)	Mean Recovered Concentration	SD	CV %	% Recovery
14.864	14.87	0.290	1.949	100.06
16.722	16/25	0.829	5.1034	97.20
18.580	18.17	0.732	4.0302	97.81

The linear regression analysis (observed vs. expected) generated the following equation:
$y= 0.9833x + 0.0344$ ($R^2= 0.9996$)

Accuracy by recovery was assessed by spiking tobramycin into human serum negative for tobramycin. The samples were analyzed in triplicate. The results are summarized below.

Theoretical Concentration (ug/mL)	Mean Recovered Concentration	SD	%CV	% Recovery
6.0	5.86	0.090	1.54	97.67
4.5	4.30	0.081	1.88	95.56
3.0	2.78	0.064	2.30	92.67
1.5	1.36	0.036	2/65	90.67

The sponsor evaluated the performance of the QMS diluent CAL A (0 ug/mL) by comparing the results of diluted samples with neat patient samples.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The QMS Tobramycin assay does not include controls or calibrators. Calibrators were cleared under k872349. The sponsor is the current owner and manufacturer of the Innofluor line and continues to manufacture the calibrators using the same validated procedures established at the time of clearance for k872349.

The sponsor performed real time stability studies to establish the 12 month shelf life claim and the 45 days on board reagent claim. Real time studies for extending the shelf life are ongoing. The protocol for establishing stability was reviewed and found to be acceptable.

d. *Detection limit:*
The analytical sensitivity (Limit of the Blank) claim of 0.17 ug/mL is defined by the sponsor as the lowest concentration of analyte detectable from zero with 95% confidence when performing the assay.

The functional sensitivity, or Limit of Quantitation, claim of 0.37 ug/mL is defined by the sponsor as the lowest concentration of analyte that can be reliably detected and at which the total error meets accuracy requirements. The low end of the claimed measuring range is 0.4 µg/mL.

e. *Analytical specificity:*
Interference testing was conducted in duplicate or triplicate using the QMS Tobramycin assay. This assay showed less than a 10% error in detecting tobramycin for the following interfering substances:

Endogenous Interfering Substance	Spiked Concentration of Tobramycin	Interfering Substance	Spiked Concentration of Tobramycin
Albumin	8.0 µg/mL	HAMA Type-1	8.0 µg/mL
Bilirubin	8.0 µg/mL	HAMA Type-2	8.0 µg/mL
Cholesterol	7.0 µg/mL	Uric Acid	7.0 µg/mL
Gamma Globulins (IgG)	7.0 µg/mL	Rheumatoid Factor	7.0 µg/mL
Hemoglobin	8.0 µg/mL	Triglyceride	7.5 µg/mL
Hemoglobin	8.0 µg/mL		

The following compounds were tested for cross-reactivity:

Cross-reactant Drug	Spiked Concentration of Tobramycin	Drug Concentration Tested (ug/mL)	Percent Cross-Reactivity
5-Fluorocytosine	6.0 µg/mL	30	0.29
Acetaminophen	6.0 µg/mL	200	Not Detect.
Amikacin	6.0 µg/mL	200	12.41
Amphotericin B	6.0 µg/mL	100	Not Detect.
Ampicillin	6.0 µg/mL	50	Not Detect.
Carbenicillin	6.0 µg/mL	2500	-0.13
Cefamandole Nafate	6.0 µg/mL	250	Not Detect.
Cephalexin	6.0 µg/mL	320	Not Detect.
Cephalosporin C	6.0 µg/mL	1000	Not Detect.
Cephalothin	6.0 µg/mL	1000	Not Detect.
Chloramphenicol	6.0 µg/mL	250	Not Detect.
Clindamycin	6.0 µg/mL	2000	Not Detect.
Ephedrine	6.0 µg/mL	1000	Not Detect.
Erythromycin	6.0 µg/mL	500	Not Detect.
Ethacrynic Acid	6.0 µg/mL	400	Not Detect.

Cross-reactant Drug	Spiked Concentration of Tobramycin	Drug Concentration Tested (ug/mL)	Percent Cross-Reactivity
Furosemide	6.0 µg/mL	100	Not Detect.
Fusidic Acid	6.0 µg/mL	1000	Not Detect.
Gentamicin	6.0 µg/mL	100	Not Detect.
Ibuprofen	6.0 µg/mL	7000	Not Detect.
Kanamycin A	6.0 µg/mL	400	6.86
Kanamycin B	6.0 µg/mL	400	6.61

Cross-reactant Drug	Spiked Concentration of Tobramycin	Drug Concentration Tested (ug/mL)	Percent Cross-Reactivity
Lincomycin	6.0 µg/mL	2000	Not Detect.
Methicillin	6.0 µg/mL	200	-0.25
Methotrexate	6.0 µg/mL	500	Not Detect.
Methylprednisolone	6.0 µg/mL	200	Not Detect.
Neomycin	6.0 µg/mL	1000	Not Detect.
Netilmycin	6.0 µg/mL	125	Not Detect.
Oxytetracycline	6.0 µg/mL	2000	Not Detect.
Penicillin V	6.0 µg/mL	100	-0.20
Prednisolone	6.0 µg/mL	12	-0.33
Rifampicin	6.0 µg/mL	500	Not Detect.
Sisomycin	6.0 µg/mL	100	Not Detect.
Spectinomycin	6.0 µg/mL	100	Not Detect.
Streptomycin	6.0 µg/mL	400	Not Detect.
Sulfadiazine	6.0 µg/mL	1000	Not Detect.
Sulfamethoxazole	6.0 µg/mL	400	Not Detect.
Tetracycline	6.0 µg/mL	2000	Not Detect.
Trimethoprim	6.0 µg/mL	200	-0.70
Vancomycin	6.0 µg/mL	400	Not Detect.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Sixty-seven purchased clinical samples were tested on a commercially available analyzer; the results ranged from 0.08 µg/mL to 9.73 µg/mL. A regression analysis was performed comparing new device results to predicate device results. Results of the analysis gave the following linear regression

statistics: y = 0.98x – 0.09; r = 0.992

b. Matrix *comparison:*

A study was conducted to determine the performance of the assay for serum and plasma samples containing tobramycin.

Blood was drawn from ten healthy donors (with no tobramycin therapy) for each tube type listed below:

- Plastic K2 EDTA tube
- Glass K3 EDTA tube
- Glass plasma separator lithium heparin tube
- Glass sodium heparin tube
- Glass lithium heparin tube
- Glass serum separator tube
- Plastic tube with clot activator
- Glass tube with no additives
- Plastic tube with no additives.

The serum or plasma was removed from the collection tubes and aliquoted into new tubes for testing (using the same procedure the customer would follow). Serum or plasma from each tube was spiked with tobramycin obtained from a supplier. These samples were analyzed on the Hitachi 917 analyzer in duplicate with baseline results obtained on day zero for each type of tube. The results showed there were no interferences with regard to the recovery of tobramycin in serum or plasma for the nine tube types tested.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Nota applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The package insert cites references (listed below) stating that therapeutic tobramycin peak serum levels of 5 to 8 µg/mL and trough levels of 1 to 2 ug/mL

have been reported for serious bacterial infections. A therapeutic range of 2 to 8 ug/mL has been suggested for tobramycin. Due to great individual differences in dosage requirements to achieve efficacious therapy as well as reported adverse effects at concentrations of 5 to 8 ug/mL, determination of tobramycin serum concentrations is required to optimize therapeutic drug management.

Burtis C, Ashwood E. Tietz N. *Clinical Guide to Laboratory Tests.* 2nd ed.

Hammett-Stable CA and Johns T. Laboratory guidelines for monitoring antimicrobial drugs. *Clinical Chemistry*. Volume 44 Issue 5, 1998: 1129-1140.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.